

SEQUENCE LISTING



<110> Copley, Clive G

Edge, Michael Derek

Emery, Stephen Charles

<120> Monoclonal Antibody to CEA, Conjugates Comprising Said Antibody,
and Their Therapeutic use in an Adept System

<130> 1991-209

<140> US 09/910,059

<141> 2001-07-23

<150> US 09/171,945

<151> 1998-10-29

<150> PCT/GB97/01165

<151> 1997-04-29

<150> GB 9703103.3

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<150> GB9609405.7

<151> 1996-05-04

<160> 131

<170> PatentIn version 3.1

<210> 1

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32

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<220>

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31

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<211> 34

<212> PRT

<213> Mus musculus

<400> 3

Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Ser Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asn
20 25 30

Tyr Met

<210> 4

<211> 24

<212> DNA

<213> Artificial Sequence

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<223> light chain cDNA backward primer

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gacattcagc tgacccagtc tcca

24

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<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> light chain cDNA backward primer

<400> 5

gacattgagc tcacccagtc tcca

24

<210> 6

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> heavy chain cDNA backward primer

<400> 6

aggtsmarct gcagsagtcw gg

22

<210> 7

<211> 41

<212> DNA

<213> Artificial Sequence

<220>

<223> heavy chain cDNA backward primer

<400> 7

actagtggaa ttcagtgtga ggtscarctg cagcartcw g

41

<210> 8

<211> 357

<212> DNA

<213> Mus musculus

<400> 8

gacattgagc tcacccagtc tccagcaatc atgtctgcat ctccagggga gaaggctacc 60

ataacctgca gtgccagctc aagtgttaact tacatgcact gggtccagca gaagccaggc 120

acttctccca aactctggat ttatagcaca tccaacctgg cttctggagt cctgctcgc 180

ttcagtggca gtggatctgg gacctcttac tctctcacia tcagccgaat ggaggctgaa 240

gatgctgccca cttattactg ccagcaaagg agtacttacc cgctcacgtt cggtgctggg 300
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<210> 9

<211> 108

<212> PRT

<213> Mus musculus

<400> 9

Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
 1 5 10 15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Thr Tyr Met
 20 25 30

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
 35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Thr Tyr Pro Leu Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala
 100 105

<210> 10

<211> 360

<212> DNA

<213> Mus musculus

<400> 10
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tcctgcacag cttctgggtt caacattaaa gacaactata tgcactgggt gaagcagagg 120
cctgaacagg gcctggagtg gattgcatgg attgatacctg agaatgggtga tactgaatat 180
gccccgaagt tccggggcaa ggccactttg actgcagact catcctccaa cacagcctac 240
ctgcacctca gcagcctgac atctgaggac actgccgtct attactgtca tgtcctgata 300
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<210> 11

<211> 120

<212> PRT

<213> Mus musculus

<400> 11

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1				5					10					15	
Ser	Val	Lys	Leu	Ser	Cys	Thr	Ala	Ser	Gly	Phe	Asn	Ile	Lys	Asp	Asn
			20					25					30		
Tyr	Met	His	Trp	Val	Lys	Gln	Arg	Pro	Glu	Gln	Gly	Leu	Glu	Trp	Ile
		35					40					45			
Ala	Trp	Ile	Asp	Pro	Glu	Asn	Gly	Asp	Thr	Glu	Tyr	Ala	Pro	Lys	Phe
	50					55					60				
Arg	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Ser	Ser	Ser	Asn	Thr	Ala	Tyr
65					70					75					80
Leu	His	Leu	Ser	Ser	Leu	Thr	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Ser Val Ala Val Ser Ser
 115 120

<210> 12

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> light chain primer

<400> 12

aagctttccc gcggggacat tgagctcacc cagtctcca

39

<210> 13

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> light chain primer

<400> 13

aagcttctcg agcttggtcc cagcaccgaa

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<210> 14

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> heavy chain primer

<400> 14

aagcttggaa ttcagtgtga ggtgcagctg cagcag

36

<210> 15

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> heavy chain primer

<400> 15

aagcttcgag ctcacggcga ctgaggttcc ttg

33

<210> 16

<211> 705

<212> DNA

<213> Artificial Sequence

<220>

<223> chimaeric light chain sequence

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cgcgggggaca ttgagctcac ccagtctcca gcaatcatgt ctgcatctcc aggggagaag 120

gtcaccataa cctgcagtgc cagctcaagt gtaacttaca tgcactgggtt ccagcagaag 180

ccaggcactt ctcccaaact ctggatttat agcacatcca acctggcttc tggagtcctt 240

gctcgcttca gtggcagtgg atctgggacc tcttactctc tcacaatcag ccgaatggag 300

gctgaagatg ctgccactta ttactgccag caaaggagta cttacccgct cacgttcggt 360
gctgggacca agctcgagat caaacggact gtggctgcac catctgtctt catcttcccg 420
ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc 480
tatcccagag aggccaaagt acagtggaag gtggataacg cctccaatc gggtaactcc 540
caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg 600
acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag 660
ggcctgagtt cgcccgtcac aaagagcttc aacaggggag agtgt 705

<210> 17

<211> 235

<212> PRT

<213> Artificial Sequence

<220>

<223> chimaeric light chain sequence

<400> 17

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Gly Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile
20 25 30

Met Ser Ala Ser Pro Gly Glu Lys Val Thr Ile Thr Cys Ser Ala Ser
35 40 45

Ser Ser Val Thr Tyr Met His Trp Phe Gln Gln Lys Pro Gly Thr Ser
50 55 60

Pro Lys Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile

85

90

95

Ser Arg Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg
 100 105 110

Ser Thr Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile Lys
 115 120 125

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
 130 135 140

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 145 150 155 160

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 165 170 175

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 180 185 190

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 195 200 205

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 210 215 220

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 18

<211> 765

<212> DNA

<213> Artificial Sequence

<220>

<223> chimaeric HuIgG2 Fd construct

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<400> 18
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gtgcagctgc agcartcagg ggcagagctt gtgaggtcag gggcctcagt caagttgtcc      120
tgcacagctt ctggcttcaa cattaaagac aactatatgc actgggtgaa gcagaggcct      180
gaacagggcc tggagtggat tgcattggatt gatcctgaga atgggtgatac tgaatatgcc      240
ccgaagttcc ggggcaaggc cactttgact gcagactcat cctccaacac agcctacctg      300
cacctcagca gcctgacatc tgaggacact gccgtctatt actgtcatgt cctgatctat      360
gctggttatt tggctatgga ctactggggt caaggaacct cagtcgccgt gagctcggct      420
agcaccaagg gaccatcggg cttccccctg gccccctgct ccaggagcac ctccgagagc      480
acagccgccc tgggctgcct ggtcaaggac tacttccccg aaccggtgac ggtgtcgtgg      540
aactcaggcg ctctgaccag cggcgtgcac accttccccg ctgtcctaca gtcctcagga      600
ctctactccc tcagcagcgt cgtgacgggtg ccctccagca acttcggcac ccagacctac      660
acctgcaacg tagatcaciaa gccagcaac accaaggtgg acaagacagt tgagcgcaaa      720
tgttgtgtcg agtgcccacc gtgcccggcg ccacctgtgg ccggc      765

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<210> 19

<211> 255

<212> PRT

<213> Artificial Sequence

<220>

<223> chimaeric HuIgG2 Fd construct

<400> 19

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Met Lys Leu Trp Leu Asn Trp Ile Phe Leu Val Thr Leu Leu Asn Gly
1           5           10           15

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Ile Gln Cys Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg
20           25           30

```

Ser Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile
 35 40 45
 Lys Asp Asn Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu
 50 55 60
 Glu Trp Ile Ala Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala
 65 70 75 80
 Pro Lys Phe Arg Gly Lys Ala Thr Leu Thr Ala Asp Ser Ser Ser Asn
 85 90 95
 Thr Ala Tyr Leu His Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val
 100 105 110
 Tyr Tyr Cys His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr
 115 120 125
 Trp Gly Gln Gly Thr Ser Val Ala Val Ser Ser Ala Ser Thr Lys Gly
 130 135 140
 Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
 145 150 155 160
 Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 165 170 175
 Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 180 185 190
 Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 195 200 205
 Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val
 210 215 220
 Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys
 225 230 235 240

Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
 245 250 255

<210> 20

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> chimaeric HuIgG1CH1' Fd construct

<400> 20

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
 1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
 20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
 35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
 65 70 75 80

Tyr Ile Cys Asn Val Asn His Asn Pro Ser Asn Thr Lys Val Asp Lys
 85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
 100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro
 115 120

<210> 21
 <211> 369
 <212> DNA
 <213> Artificial Sequence

<220>

<223> chimaeric HuIgG1CH1' Fd construct

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 ggcacagcgg ccctgggctg cctgggtcaag gactacttcc ccgaaccggg gacgggtgtcg 120
 tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180
 ggactctact ccctcagcag cgtgggtgact gtgccctcca gcagcttggg caccagacc 240
 tacatctgca acgtgaatca caaccccagc aacaccaagg tcgacaagaa agttgagccc 300
 aaatcttgtg acaagacgca cacgtgcccg ccgtgcccgg ctccggaact gctgggtggc 360
 ccgtaatag 369

<210> 22
 <211> 116
 <212> PRT
 <213> Homo sapiens

<400> 22

Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Cys	Ser	Arg
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Ser	Thr	Ser	Glu	Ser	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr
			20					25					30		
Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser
		35					40					45			

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr
 65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
 85 90 95

Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro
 100 105 110

Pro Val Ala Gly
 115

<210> 23

<211> 348

<212> DNA

<213> Homo sapiens

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 agcacagccg ccctgggctg cctgggtcaag gactacttcc ccgaaccggt gacgggtgtcg 120
 tggaactcag gcgctctgac cagcggcgtg cacaccttcc cggtgttcct acagtcctca 180
 ggactctact ccctcagcag cgtcgtgacg gtgccctcca gcaacttcgg caccagacc 240
 tacacctgca acgtagatca caagcccagc aacaccaagg tggacaagac agttgagcgc 300
 aaatgttggtg tcgagtgcc accgtgcccg gcgccacctg tggccggc 348

<210> 24

<211> 167

<212> PRT

<213> Artificial Sequence

<220>

<223> chimaeric HuIgG3CH1' Fd construct

<400> 24

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Thr Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Leu Lys Thr Pro Leu Gly Asp Thr Thr His Thr Cys Pro
100 105 110

Arg Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg
115 120 125

Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys
130 135 140

Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro
145 150 155 160

Ala Pro Glu Leu Leu Gly Gly
165

<210> 25

<211> 501

<212> DNA

<213> Artificial Sequence

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<223> chimaeric HuIgG3CH1' Fd construct

<400> 25

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tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca     180
ggactctact ccctcagcag cgtgggtgacc gtgccctcca gcagcttggg caccagacc      240
tacacctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agtggagctg      300
aaaaccccac ttggtgacac aactcacacg tgccctaggt gtcctgaacc taaatcttgt      360
gacacacctc ccccgtgccc acggtgcccga gagcccaaat cttgcgacac gccccaccg      420
tgtcccagat gtcctgaacc aaagagctgt gacactccac cgccctgccc gaggtgcccga     480
gcacctgaac tcctgggagg a                                           501
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<210> 26

<211> 10

<212> PRT

<213> Mus musculus

<400> 26

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1           5           10
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<210> 27

<211> 7

<212> PRT

<213> Mus musculus

<400> 27

Ser Thr Ser Asn Leu Ala Ser
1 5

<210> 28

<211> 9

<212> PRT

<213> Mus musculus

<400> 28

Gln Gln Arg Ser Thr Tyr Pro Leu Thr
1 5

<210> 29

<211> 5

<212> PRT

<213> Mus musculus

<400> 29

Asp Asn Tyr Met His
1 5

<210> 30

<211> 9

<212> PRT

<213> Mus musculus

<400> 30

Phe Asn Ile Lys Asp Asn Tyr Met His
1 5

<210> 31

<211> 17

<212> PRT

<213> Mus musculus

<400> 31

Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Lys Phe Arg
1 5 10 15

Gly

<210> 32

<211> 11

<212> PRT

<213> Mus musculus

<400> 32

Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr
1 5 10

<210> 33

<211> 13

<212> PRT

<213> Mus musculus

<400> 33

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr
1 5 10

<210> 34

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> polylinker sequence

<400> 34
tcgagagatc taagcttccg cgggaattcc tcgaggagct ccccggggga tccgtcgact 60

<210> 35

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> polylinker sequence

<400> 35
ctagagtcga cggatccccc ggggagctcc tcgaggaatt cccgcggaag cttagatctc 60

<210> 36

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> polyA region PCR primer

<400> 36

aagcttccccg ggtattaaag cagaacttg

29

<210> 37

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> polyA region PCR primer

<400> 37

actagtggat cccagacatg ataagatac

29

<210> 38

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> mutagenesis PCR primer

<400> 38

ggtctatata agcagagctg tctggctaac tagagaacc

39

<210> 39

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> mutagenesis PCR primer

<400> 39

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39

<210> 40

<211> 19

<212> DNA

<213> Artificial Sequence

<220>

<223> flanking PCR primer

<400> 40

ggactttcct acttggcag

19

<210> 41

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> flanking PCR primer

<400> 41

ggcaactaga aggcacagtc

20

<210> 42

<211> 77

<212> DNA

<213> Artificial Sequence

<220>

<223> Kozak recognition and light chain signal sequences

<400> 42

agcttgccgc caccatggat tttcaagtcg agattttcag cttcctgcta atcagtgctt 60

cagtcataat gtcccg 77

<210> 43

<211> 71

<212> DNA

<213> Artificial Sequence

<220>

<223> Kozak recognition and light chain signal sequences

<400> 43

gggacattat gactgaagca ctgattagca ggaagctgaa aatctgcact tgaaaatcca 60

tggtggcggc a 71

<210> 44

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> Kozak recognition and heavy chain signal sequences

<400> 44
agcttgccgc caccatgaag ttgtggctga actggatttt ccttgtaaca cttttaaatg 60
g 61

<210> 45

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> Kozak recognition and heavy chain signal sequences

<400> 45
aattccattt aaaagtgtta caaggaaaat ccagttcagc cacaacttca tgggtggcggc 60
a 61

<210> 46

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> human light chain kappa constant region insert

<400> 46
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gatgagcagt tgaaatctgg aactgcctct gttgtgtgcc tgctgaataa cttctatccc 120
agagaggcca aagtacagtg gaaggtggat aacgccctcc aatcgggtaa ctcccaggag 180
agtgtcacag agcaggacag caaggacagc acctacagcc tcagcagcac cctgacgctg 240
agcaaagcag actacgagaa acacaaagtc tacgcctgcg aagtcaccca tcagggcctg 300
agttcgcccc tcacaaagag cttcaacagg ggagagtgtt aatagcccgg gactagt 357

<210> 47

<211> 381

<212> DNA

<213> Artificial Sequence

<220>

<223> human heavy chain 1gG2CH1 constant region insert

<400> 47

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ccggtgacgg tgtcgtggaa ctcaggcgct ctgaccagcg gcgtgcacac cttcccggct      180
gtcctacagt cctcaggact ctactccctc agcagcgtcg tgacggtgcc ctccagcaac      240
ttcggcaccc agacctacac ctgcaacgta gatcacaagc ccagcaacac caaggtggac      300
aagacagttg agcgcaaatg ttgtgtcgag tgcccaccgt gcccggcgcc acctgtggcc      360
ggctaatagc ccgggactag t                                     381
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<210> 48

<211> 342

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised antibody variable region

<400> 48

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aagctttccc gcggcgacat ccagatgacc cagagcccaa gcagcctgag cgctagcgtg      60
ggtgacagag tgaccatcac gtgtagtgcc agctcaagtg taacttacat gcactgggtac      120
cagcagaagc caggtaaggc tccaaagctg ctgatctaca gcacatccaa cctggcttct      180
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ggtgtgccaa gcagattctc cggaagcggg agcggcaccg actacacctt caccatcagc	240
agcctccagc cagaggatat cgccacctac tactgccagc agaggagtagc ttacccgctc	300
acgttcggcc aagggaacaa gctcgagatc aaacggacta gt	342

<210> 49

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> humanized light chain variable region

<400> 49

gacatccaga tgacccagag cccaagcagc ctgagcgcta gcgtgggtga cagagtgacc	60
atcacgtgta gtgccagctc aagtgttaact tacatgcact ggtaccagca gaagccaggt	120
aaggctccaa agctgctgat ctacagcaca tccaacctgg cttctggtgt gccaagcaga	180
ttctccggaa gcggtagcgg caccgactac accttcacca tcagcagcct ccagccagag	240
gatatcgcca cctactactg ccagcagagg agtacttacc cgctcacgtt cggccaaggg	300
accaagctcg agatcaaacg g	321

<210> 50

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> humanized light chain variable region

<400> 50

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

1	5	10	15
Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Thr Tyr Met	20	25	30
His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr	35	40	45
Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser	50	55	60
Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu	65	70	75
Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Thr Tyr Pro Leu Thr	85	90	95
Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg	100	105	

<210> 51

<211> 705

<212> DNA

<213> Artificial Sequence

<220>

<223> complete humanised light chain sequence

<400> 51

atggattttc aagtgcagat tttcagcttc ctgctaataca gtgcttcagt cataatgtcc	60
cgcgggcgaca tccagatgac ccagagccca agcagcctga gcgctagcgt ggggtgacaga	120
gtgaccatca cgtgtagtgc cagctcaagt gtaacttaca tgcactggta ccagcagaag	180
ccaggtaagg ctccaaagct gctgatctac agcacatcca acctggcttc tgggtgtgcca	240
agcagattct ccggaagcgg tagcggcacc gactacacct tcaccatcag cagcctccag	300

ccagaggata tcgccaccta ctactgccag cagaggagta cttacccgct cacgttcggc 360
caagggacca agctcgagat caaacggact gtggctgcac catctgtctt catcttccc 420
ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc 480
tatcccagag aggccaaagt acagtggaag gtggataacg cctccaatc gggtaactcc 540
caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcacctg 600
acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag 660
ggcctgagtt cgcccgtcac aaagagcttc aacaggggag agtgt 705

<210> 52

<211> 235

<212> PRT

<213> Artificial Sequence

<220>

<223> complete humanised light chain sequence

<400> 52

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser
35 40 45

Ser Ser Val Thr Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile

85

90

95

Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Arg
 100 105 110

Ser Thr Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 115 120 125

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
 130 135 140

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 145 150 155 160

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 165 170 175

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 180 185 190

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 195 200 205

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 210 215 220

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 53

<211> 385

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain PCR fragment

<400> 53
gaagcttgga attcagtgtg aggtgcagct gcagcagagc ggtccaggtc tcgtacggcc 60
tagccagacc ctgagcctca cgtgcaccgc atctggcttc aacattaagg acaattacat 120
gcaactgggtg agacagccac ctggacgagg ccttgagtgg attggatgga ttgaccctga 180
gaatgggtgac actgagtacg cacctaagtt tcgcggccgc gtgacaatgc tggcagacac 240
tagtaagaac cagttcagcc tgagactcag cagcgtgaca gccgccgaca ccgcggtcta 300
ttattgtcac gtcctgatat acgccgggta tctggcaatg gactactggg gcccaaggga 360
cctcgtcacc gtgagctcga ctagt 385

<210> 54

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised antibody variable region

<400> 54
gaggtgcagc tgcagcagag cgggtccaggc ctcgtacggc ctagccagac cctgagcctc 60
acgtgcaccg catctggctt caacattaag gacaattaca tgcactgggt gagacagcca 120
cctggacgag gccttgagtg gattggatgg attgaccctg agaatgggtga cactgagtac 180
gcacctaagt ttcgcggccg cgtgacaatg ctggcagaca ctagtaagaa ccagttcagc 240
ctgagactca gcagcgtgac agccgccgac accgcggtct attattgtca cgtcctgata 300
tacgccgggt atctggcaat ggactactgg ggccaaggga ccctcgtcac cgtgagctcg 360

<210> 55

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised antibody variable region

<400> 55

Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asn
20 25 30

Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
35 40 45

Gly Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Lys Phe
50 55 60

Arg Gly Arg Val Thr Met Leu Ala Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 56

<211> 765

<212> DNA

<213> Artificial Sequence

<220>

<223> complete humanised Fd heavy chain sequence

<400> 56
atgaagttgt ggctgaactg gattttcctt gtaacacttt taaatggaat tcagtgtgag 60
gtgcagctgc agcagagcgg tccaggtctc gtacggccta gccagaccct gagcctcacg 120
tgcaccgcat ctggcttcaa cattaaggac aattacatgc actgggtgag acagccacct 180
ggacgaggcc ttgagtggat tggatggatt gaccctgaga atggtgacac tgagtacgca 240
cctaagtttc gcggccgcgt gacaatgctg gcagacacta gtaagaacca gttcagcctg 300
agactcagca gcgtgacagc cgccgacacc gcggtctatt attgtcacgt cctgatatac 360
gccgggtatc tggcaatgga ctactggggc caagggaccc tcgtcaccgt gagctcggct 420
agcaccaagg gaccatcggg cttccccctg gccccctgct ccaggagcac ctccgagagc 480
acagccgccc tgggctgcct ggtcaaggac tacttccccg aaccggtgac ggtgtcgtgg 540
aactcaggcg ctctgaccag cggcgtgcac accttccccg ctgtcctaca gtectcagga 600
ctctactccc tcagcagcgt cgtgacggtg ccctccagca acttcggcac ccagacctac 660
acctgcaacg tagatcaciaa gccagcaac accaaggtgg acaagacagt tgagcgcaaa 720
tgttgtgtcg agtgcccacc gtgcccggcg ccacctgtgg ccggc 765

<210> 57

<211> 255

<212> PRT

<213> Artificial Sequence

<220>

<223> complete humanised Fd heavy chain sequence

<400> 57

Met	Lys	Leu	Trp	Leu	Asn	Trp	Ile	Phe	Leu	Val	Thr	Leu	Leu	Asn	Gly
1				5					10					15	

Ile	Gln	Cys	Glu	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Gly	Leu	Val	Arg
			20					25					30		

Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile
 35 40 45
 Lys Asp Asn Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu
 50 55 60
 Glu Trp Ile Gly Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala
 65 70 75 80
 Pro Lys Phe Arg Gly Arg Val Thr Met Leu Ala Asp Thr Ser Lys Asn
 85 90 95
 Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
 100 105 110
 Tyr Tyr Cys His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr
 115 120 125
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 130 135 140
 Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser
 145 150 155 160
 Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 165 170 175
 Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 180 185 190
 Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 195 200 205
 Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val
 210 215 220
 Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys
 225 230 235 240

Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly
 245 250 255

<210> 58

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant insert

<400> 58

ggcgacatcc agctgaccca gagcccaagc agcctgagcg

40

<210> 59

<211> 46

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant insert

<400> 59

ctagcgctca ggctgcttgg gctctggggtc agctggatgt cgccgc

46

<210> 60

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant

<400> 60
gacatccagc tgacccagag cccaagcagc ctgagcgcta gcgtgggtga cagagtgacc 60
atcacgtgta gtgccagctc aagtgttaact tacatgcact ggtaccagca gaagccaggt 120
aaggctccaa agctgctgat ctacagcaca tccaacctgg cttctggtgt gccaagcaga 180
ttctccggaa gcggtagcgg caccgactac accttcacca tcagcagcct ccagccagag 240
gatatcgcca cctactactg ccagcagagg agtacttacc cgctcacgtt cggccaaggg 300
accaagctcg agatcaaacg g 321

<210> 61

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant

<400> 61

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Thr Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Thr Tyr Pro Leu Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
100 105

<210> 62

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant

<400> 62

ggccagatcg tgctgaccca gagcccaagc agcctgagcg

40

<210> 63

<211> 46

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant

<400> 63

ctagcgctca ggctgcttgg gctctgggtc agcacgatct ggccgc

46

<210> 64

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant

<400> 64

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cagatcgtgc tgaccagag cccaagcagc ctgagcgcta gcgtgggtga cagagtgacc      60
atcacgtgta gtgccagctc aagtgttaact tacatgcact ggtaccagca gaagccaggt      120
aaggctccaa agctgctgat ctacagcaca tccaacctgg cttctggtgt gccaagcaga      180
ttctccggaa gcggtagcgg caccgactac accttcacca tcagcagcct ccagccagag      240
gatatcgcca cctactactg ccagcagagg agtacttacc cgctcacgtt cggccaaggg      300
accaagctcg agatcaaacg g                                     321
```

<210> 65

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant

<400> 65

```
Gln Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1           5           10           15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Thr Tyr Met
          20           25           30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
          35           40           45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
          50           55           60

Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu
```

65		70		75		80									
Asp	Ile	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Arg	Ser	Thr	Tyr	Pro	Leu	Thr
				85					90					95	

Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg
			100					105		

<210> 66

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for variable region variant

<400> 66

cgtattagtc atcgctatta cc

22

<210> 67

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for variable region variant

<400> 67

gttgatgtg ctgtagatcc acagctttgg agccttacc

39

<210> 68

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for variable region variant

<400> 68

tccgtttgat ctcgagcttg g

21

<210> 69

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for variable region variant

<400> 69

ggtaaggctc caaagctgtg gatctacagc acatccaac

39

<210> 70

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant

<400> 70

gacatccaga tgacccagag cccaagcagc ctgagcgcta gcgtgggtga cagagtgacc 60

atcacgtgta gtgccagctc aagtgttaact tacatgcact ggtaccagca gaagccaggt 120

aaggctccaa agctgtggat ctacagcaca tccaacctgg cttctggtgt gccaagcaga 180

ttctccggaa gcggtagcgg caccgactac accttcacca tcagcagcct ccagccagag 240

gatatcgcca cctactactg ccagcagagg agtacttacc cgctcacgtt cggccaaggg 300
 accaagctcg agatcaaacg g 321

<210> 71

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised light chain variable region variant

<400> 71

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Thr Tyr Met
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr
 35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu
 65 70 75 80

Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Thr Tyr Pro Leu Thr
 85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
 100 105

<210> 72

<211> 64

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant insert

<400> 72

ccttgagtgg attgcatgga ttgaccctga gaatggtgac actgagtacg cacctaagtt 60

tcgc 64

<210> 73

<211> 68

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant insert

<400> 73

ggccgcgaaa cttaggtgcg tactcagtgt caccattctc aggggtcaatc catgcaatcc 60

actcaagg 68

<210> 74

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant

<400> 74

gaggtgcagc tgcagcagag cgggtccaggt ctcgtacggc ctagccagac cctgagcctc 60

acgtgcaccg catctggctt caacattaag gacaattaca tgcactgggt gagacagcca 120
 cctggacgag gccttgagtg gattgcatgg attgaccctg agaatgggtga cactgagtac 180
 gcacctaagt ttcgcgggccg cgtgacaatg ctggcagaca ctagtaagaa ccagttcagc 240
 ctgagactca gcagcgtgac agccgcccac accgcggtct attattgtca cgtcctgata 300
 tacgccgggt atctggcaat ggactactgg ggccaaggga ccctcgtcac cgtgagctcg 360

<210> 75

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant

<400> 75

Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asn
 20 25 30

Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
 35 40 45

Ala Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Lys Phe
 50 55 60

Arg Gly Arg Val Thr Met Leu Ala Asp Thr Ser Lys Asn Gln Phe Ser
 65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln

100

105

110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 76

<211> 80

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant insert

<400> 76

ggccgcgtga caatgctggc agactcaagt aagaaccagg ccagcctgag actcagcagc 60

gtgacagccg ccgacaccgc 80

<210> 77

<211> 74

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant insert

<400> 77

gggtgcggcg gctgtcacgc tgctgagtct caggctggcc tggttcttac ttgagtctgc 60

cagcattgtc acgc 74

<210> 78

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant

<400> 78

```
gaggtgcagc tgcagcagag cgggtccaggt ctcgtacggc ctagccagac cctgagcctc      60
acgtgcaccg catctggctt caacattaag gacaattaca tgcactgggt gagacagcca      120
cctggacgag gccttgagtg gattggatgg attgaccctg agaatgggtga cactgagtac      180
gcacctaagt ttcgcggccg cgtgacaatg ctggcagact caagtaagaa ccaggccagc      240
ctgagactca gcagcgtgac agccgccgac accgcggtct attattgtca cgtcctgata      300
tacgccgggt atctggcaat ggactactgg ggccaaggga ccctcgtcac cgtgagctcg      360
```

<210> 79

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant

<400> 79

```
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1          5          10          15

Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asn
20        25        30

Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
35        40        45

Gly Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Lys Phe
50        55        60
```

Arg Gly Arg Val Thr Met Leu Ala Asp Ser Ser Lys Asn Gln Ala Ser
 65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 80

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant

<400> 80

gaggtgcagc tgcagcagag cgggtccaggt ctcgtacggc ctagccagac cctgagcctc	60
acgtgcaccg catctggctt caacattaag gacaattaca tgcactgggt gagacagcca	120
cctggacgag gccttgagtg gattgcatgg attgaccctg agaatgggtga cactgagtac	180
gcacctaagt ttcgcggccg cgtgacaatg ctggcagact caagtaagaa ccaggccagc	240
ctgagactca gcagcgtgac agccgccgac accgcggtct attattgtca cgtcctgata	300
tacgccgggt atctggcaat ggactactgg ggccaaggga ccctcgtcac cgtgagctcg	360

<210> 81

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant

<400> 81

Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asn
20 25 30

Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
35 40 45

Ala Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Lys Phe
50 55 60

Arg Gly Arg Val Thr Met Leu Ala Asp Ser Ser Lys Asn Gln Ala Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 82

<211> 80

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant insert

<400> 82

ggccgcgccca caatgctggc agacactagt aagaaccagt tcagcctgag actcagcagc 60

gtgacagccg ccgacaccgc 80

<210> 83

<211> 74

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region variant insert

<400> 83

ggtgtcggcg gctgtcacgc tgctgagtct caggctgaac tggttcttac tagtgtctgc 60

cagcattgtg gcgc 74

<210> 84

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region

<400> 84

gaggtgcagc tgcagcagag cgggtccaggt ctcgtacggc ctagccagac cctgagcctc 60

acgtgcaccg catctggctt caacattaag gacaattaca tgcactgggt gagacagcca 120

cctggacgag gccttgagtg gattggatgg attgaccctg agaatgggtga cactgagtac 180

gcacctaaagt ttgcgggccg cgccacaatg ctggcagaca ctagtaagaa ccagttcagc 240

ctgagactca gcagcgtgac agccgccgac accgcggtct attattgtca cgtcctgata 300

tacgccgggt atctggcaat ggactactgg ggccaaggga ccctcgtcac cgtgagctcg 360

<210> 85

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region

<400> 85

Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asn
20 25 30

Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
35 40 45

Gly Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Lys Phe
50 55 60

Arg Gly Arg Ala Thr Met Leu Ala Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 86

<211> 80
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> humanised heavy chain variable region insert

 <400> 86
 ggccgcgcca caatgctggc agactcaagt aagaaccagg ccagcctgag actcagcagc 60
 gtgacagccg ccgacaccgc 80

 <210> 87
 <211> 74
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> humanised heavy chain variable region insert

 <400> 87
 ggtgtcggcg gctgtcacgc tgctgagtct caggctggcc tggttcttac ttgagtctgc 60
 cagcattgtg gcgc 74

 <210> 88
 <211> 360
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> humanised heavy chain variable region

<400> 88
gaggtgcagc tgcagcagag cgggtccaggt ctcgtacggc ctagccagac cctgagcctc 60
acgtgcaccg catctggctt caacattaag gacaattaca tgcactgggt gagacagcca 120
cctggacgag gccttgagtg gattggatgg attgaccctg agaatgggtga cactgagtac 180
gcacctaagt ttcgcgcccg cgccacaatg ctggcagact caagtaagaa ccaggccagc 240
ctgagactca gcagcgtgac agccgcccagc accgcggtct attattgtca cgtcctgata 300
tacgccgggt atctggcaat ggactactgg ggccaaggga ccctcgtcac cgtgagctcg 360

<210> 89

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region

<400> 89

Glu	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Gly	Leu	Val	Arg	Pro	Ser	Gln
1				5					10					15	

Thr	Leu	Ser	Leu	Thr	Cys	Thr	Ala	Ser	Gly	Phe	Asn	Ile	Lys	Asp	Asn
			20					25					30		

Tyr	Met	His	Trp	Val	Arg	Gln	Pro	Pro	Gly	Arg	Gly	Leu	Glu	Trp	Ile
		35					40					45			

Gly	Trp	Ile	Asp	Pro	Glu	Asn	Gly	Asp	Thr	Glu	Tyr	Ala	Pro	Lys	Phe
	50					55					60				

Arg	Gly	Arg	Ala	Thr	Met	Leu	Ala	Asp	Ser	Ser	Lys	Asn	Gln	Ala	Ser
65					70					75					80

Leu	Arg	Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 90

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region

<400> 90

gaggtgcagc tgcagcagag cgggtccaggt ctcgtacggc ctagccagac cctgagcctc	60
acgtgcaccg catctggctt caacattaag gacaattaca tgcactgggt gagacagcca	120
cctggacgag gccttgagtg gattgcatgg attgaccctg agaatgggtga cactgagtac	180
gcacctaaagt ttgcgcggccg cgccacaatg ctggcagact caagtaagaa ccaggccagc	240
ctgagactca gcagcgtgac agccgcccag accgcggtct attattgtca cgtcctgata	300
tacgcggggt atctggcaat ggactactgg ggccaaggga ccctcgtcac cgtgagctcg	360

<210> 91

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised heavy chain variable region

<400> 91

Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asn
20 25 30

Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
35 40 45

Ala Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Lys Phe
50 55 60

Arg Gly Arg Ala Thr Met Leu Ala Asp Ser Ser Lys Asn Gln Ala Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 92

<211> 780

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised IgG1 sequence

<400> 92

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gtgcagctgc agcagagcgg tccaggtctc gtacggccta gccagaccct gagcctcacg 120

tgcaccgcat ctggcttcaa cattaaggac aattacatgc actgggtgag acagccacct 180

ggacgaggcc ttgagtggat tggatggatt gaccctgaga atggtgacac tgagtacgca 240
 cctaagtttc gcggccgcgt gacaatgctg gcagacacta gtaagaacca gttcagcctg 300
 agactcagca gcgtgacagc cgccgacacc gcggtctatt attgtcacgt cctgatatac 360
 gccgggtatc tggcaatgga ctactggggc caagggaccc tcgtcaccgt gagctcggcc 420
 tccaccaagg gcccatcggt ctccccctg gcaccctcct ccaagagcac ctctgggggc 480
 acagcggccc tgggctgcct ggtcaaggac tacttccccg aaccggtgac ggtgtcgtgg 540
 aactcaggcg ccctgaccag cggcgtgcac accttccccg ctgtcctaca gtcctcagga 600
 ctctactccc tcagcagcgt ggtgactgtg ccctccagca gcttgggcac ccagacctac 660
 atctgcaacg tgaatcaca cccagcaac accaaggtcg acaagaaagt tgagcccaaa 720
 tcttgtgaca agacgcacac gtgcccgcgc tgcccggtc cggaactgct ggggtggccc 780

<210> 93

<211> 260

<212> PRT

<213> Artificial Sequence

<220>

<223> HuVH1-HuIgG1 Fd heavy chain

<400> 93

Met	Lys	Leu	Trp	Leu	Asn	Trp	Ile	Phe	Leu	Val	Thr	Leu	Leu	Asn	Gly
1				5					10					15	

Ile	Gln	Cys	Glu	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Gly	Leu	Val	Arg
			20					25					30		

Pro	Ser	Gln	Thr	Leu	Ser	Leu	Thr	Cys	Thr	Ala	Ser	Gly	Phe	Asn	Ile
		35					40					45			

Lys	Asp	Asn	Tyr	Met	His	Trp	Val	Arg	Gln	Pro	Pro	Gly	Arg	Gly	Leu
	50					55					60				

Glu Trp Ile Gly Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala
65 70 75 80

Pro Lys Phe Arg Gly Arg Val Thr Met Leu Ala Asp Thr Ser Lys Asn
85 90 95

Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
100 105 110

Tyr Tyr Cys His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
210 215 220

Asn His Asn Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
225 230 235 240

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
245 250 255

Leu Gly Gly Pro
260

<210> 94

<211> 918

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised IgG3 heavy chain Fd sequence

<400> 94

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gtgcagctgc agcagagcgg tccaggtctc gtacggccta gccagaccct gagcctcacg	120
tgcaccgcat ctggcttcaa cattaaggac aattacatgc actgggtgag acagccacct	180
ggacgaggcc ttgagtggat tggatggatt gaccctgaga atggtgacac tgagtacgca	240
cctaagtttc gcggccgcgt gacaatgctg gcagacacta gtaagaacca gttcagcctg	300
agactcagca gcgtgacagc cgccgacacc gcggtctatt attgtcacgt cctgatatac	360
gccgggtatc tggcaatgga ctactggggc caagggaccc tcgtcacctg gagctcggct	420
agcaccaagg gcccatcggt cttccccctg gcgccctgct ccaggagcac ctctgggggc	480
acagcggccc tgggctgcct ggtcaaggac tacttccccg aaccggtgac ggtgtcgtgg	540
aactcaggcg ccctgaccag cggcgtgcac accttccccg ctgtcctaca gtcctcagga	600
ctctactccc tcagcagcgt ggtgaccgtg ccctccagca gcttgggcac ccagacctac	660
acctgcaacg tgaatcacia gccagcaac accaaggtgg acaagagagt ggagctgaaa	720
acccactcg gtgacacaac tcacacgtgc cctaggtgtc ctgaacctaa atcttgtgac	780
acacctcccc cgtgcccacg gtgcccagag cccaaatctt gcgacacgcc cccaccgtgt	840
cccagatgtc ctgaacaaaa gagctgtgac actccaccgc cctgcccagag gtgcccagca	900
cctgaactcc tgggaggg	918

<210> 95

<211> 306

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised IgG3 heavy chain Fd sequence

<400> 95

Met Lys Leu Trp Leu Asn Trp Ile Phe Leu Val Thr Leu Leu Asn Gly
1 5 10 15

Ile Gln Cys Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg
20 25 30

Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile
35 40 45

Lys Asp Asn Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu
50 55 60

Glu Trp Ile Gly Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala
65 70 75 80

Pro Lys Phe Arg Gly Arg Val Thr Met Leu Ala Asp Thr Ser Lys Asn
85 90 95

Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
100 105 110

Tyr Tyr Cys His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Gly Gly
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Thr Cys Asn Val
210 215 220

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Leu Lys
225 230 235 240

Thr Pro Leu Gly Asp Thr Thr His Thr Cys Pro Arg Cys Pro Glu Pro
245 250 255

Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu Pro Lys
260 265 270

Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu Pro Lys Ser
275 280 285

Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Ala Pro Glu Leu Leu
290 295 300

Gly Gly
305

<210> 96

<211> 705

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain Fd sequence

<400> 96

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atggattttc aagtgcagat tttcagcttc ctgctaataca gtgcttcagt cataatgtcc      60
cgcgggccaga tcgtgctgac ccagagccca agcagcctga gcgctagcgt ggggtgacaga      120
gtgaccatca cgtgtagtgc cagctcaagt gtaacttaca tgcactggta ccagcagaag      180
ccaggtaagg ctccaaagct gctgatctac agcacatcca acctggcttc tgggtgtgcca      240
agcagattct ccggaagcgg tagcggcacc gactacacct tcaccatcag cagcctccag      300
ccagaggata tcgccaccta ctactgccag cagaggagta cttacccgct cacgttcggc      360
caagggacca agctcgagat caaacggact gtggctgcac catctgtctt catcttcccg      420
ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc      480
tatccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaactcc      540
caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg      600
acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag      660
ggcctgagtt cgcccgtcac aaagagcttc aacaggggag agtgt      705
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<210> 97

<211> 235

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised light chain Fd sequence

<400> 97

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Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1           5           10           15
```

```
Val Ile Met Ser Arg Gly Gln Ile Val Leu Thr Gln Ser Pro Ser Ser
          20           25           30
```

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser
 35 40 45
 Ser Ser Val Thr Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
 50 55 60
 Pro Lys Leu Leu Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro
 65 70 75 80
 Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile
 85 90 95
 Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Arg
 100 105 110
 Ser Thr Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 115 120 125
 Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
 130 135 140
 Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 145 150 155 160
 Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 165 170 175
 Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 180 185 190
 Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 195 200 205
 Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 210 215 220
 Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 98

<211> 705

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised light chain Fd sequence

<400> 98

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cgcgggcgaca tccagatgac ccagagccca agcagcctga gcgctagcgt gggtgacaga      120
gtgaccatca cgtgtagtgc cagctcaagt gtaacttaca tgcactggta ccagcagaag      180
ccaggtaagg ctccaaagct gtggatctac agcacatcca acctggcttc tgggtgtgcca      240
agcagattct ccggaagcgg tagcggcacc gactacacct tcaccatcag cagcctccag      300
ccagaggata tcgccaccta ctactgccag cagaggagta cttacccgct cacgttcggc      360
caagggacca agctcgagat caaacggact gtggctgcac catctgtctt catcttcccg      420
ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc      480
tatcccagag aggccaaagt acagtggaag gtggataacg ccctccaatc gggtaactcc      540
caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccttg      600
acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag      660
ggcctgagtt cgcccgtcac aaagagcttc aacaggggag agtgt                          705
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<210> 99

<211> 235

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised light chain Fd sequence

<400> 99

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser
35 40 45

Ser Ser Val Thr Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Arg
100 105 110

Ser Thr Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
115 120 125

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
130 135 140

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
145 150 155 160

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
165 170 175

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
180 185 190

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 195 200 205

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 210 215 220

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 100

<211> 54

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for humanised Fd

<400> 100

cccagcacct gaactcctgg gaggagcaac aggacacagt tatgagaagt acaa

54

<210> 101

<211> 50

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for humanised Fd

<400> 101

gggggtctag attattagta caggtgttcc aggacgtagc tggcaacata

50

<210> 102

<211> 46

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for humanised Fd

<400> 102

gggggagctc ggctagcacc aagggcccat cggtcttccc cctggc

46

<210> 103

<211> 55

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for humanised Fd

<400> 103

ttgtacttct cataactgtg tcctgttgct cctcccagga gttcaggtgc tgggc

55

<210> 104

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for humanised Fd

<400> 104

gcctgtgctc aatattgatg g

21

<210> 105

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for humanised Fd

<400> 105

ggagaaagcc atatctgcct g

21

<210> 106

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 106

tcgctattac catggtgatg cggttttggc

30

<210> 107

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 107

ggctggattc tcagtggcga ctt

23

<210> 108

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for humanised Fd

<400> 108

cacaacagag gcagttcc

18

<210> 109

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for humanised Fd

<400> 109

caccttcacc atcagcagcc

20

<210> 110

<211> 19

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for preproHCPB

<400> 110

ggacctgctg cagagtctg

19

<210> 111

<211> 47

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for preproHCPB

<400> 111

ggctgcagga attccttatta tagacgaacc cggctatcaa actgagc

47

<210> 112

<211> 1870

<212> DNA

<213> Artificial Sequence

<220>

<223> expected PCR insert

<400> 112

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60

ggaattcagt gtgaggtgca gctgcagcag agcgggtccag gtctcgtacg gcctagccag

120

accctgagcc tcacgtgcac cgcacatctggc ttcaacatta aggacaatta catgcactgg

180

gtgagacagc cacctggacg aggccttgag tggattggat ggattgaccc tgagaatggt

240

gacactgagt acgcacctaa gtttcgcggc cgcgtgacaa tgctggcaga cactagtaag

300

aaccagttca gcctgagact cagcagcgtg acagccgccg acaccgcggt ctattattgt

360

cacgtcctga tatacgcggg gtatctggca atggactact ggggccaagg gaccctcgtc

420

accgtgagct cggctagcac caagggccca tcgggtcttcc ccctggcgcc ctgctccagg

480

agcacctctg ggggcacagc ggccctgggc tgctgtgtca aggactactt ccccgaaaccg

540

gtgacggtgt	cgtggaactc	aggcgccctg	accagcggcg	tgcacacctt	cccggctgtc	600
ctacagtcct	caggactcta	ctccctcagc	agcgtggtga	ccgtgccctc	cagcagcttg	660
ggcaccacaga	cctacacctg	caacgtgaat	cacaagccca	gcaacaccaa	ggtggacaag	720
agagtggagc	tgaaaacccc	actcggtgac	acaactcaca	cgtgccctag	gtgtcctgaa	780
cctaaatctt	gtgacacacc	tcccccgtag	ccacggtgcc	cagagcccaa	atcttgcgac	840
acgccccac	cgtgtcccag	atgtcctgaa	caaagagct	gtgacactcc	accgccctgc	900
ccgaggtgcc	cagcacctga	actcctggga	ggagcaacag	gacacagtta	tgagaagtac	960
aacaagtggg	aaacgataga	ggcttggact	caacaagtcg	ccactgagaa	tccagccctc	1020
atctctcgca	gtgttatcgg	aaccacattt	gagggacgcg	ctatttacct	cctgaagggt	1080
ggcaaagctg	gacaaaataa	gcctgccatt	ttcatggact	gtggtttcca	tgccagagag	1140
tggatttctc	ctgcattctg	ccagtggttt	gtaagagagg	ctgttcgtac	ctatggacgt	1200
gagatccaag	tgacagagct	tctcgacaag	ttagactttt	atgtcctgcc	tgtgctcaat	1260
attgatggct	acatctacac	ctggaccaag	agccgatttt	ggagaaagac	tcgctccacc	1320
catactggat	ctagctgcat	tggcacagac	ccaacagaa	attttgatgc	tggttggtgt	1380
gaaattggag	cctctcgaaa	cccctgtgat	gaaacttact	gtggacctgc	cgcagagtct	1440
gaaaaggaga	ccaaggccct	ggctgatttc	atccgcaaca	aactctcttc	catcaaggca	1500
tatctgacaa	tccactcgta	ctcccaaagt	atgatctacc	cttactcata	tgcttacaaa	1560
ctcggtgaga	acaatgctga	gttgaatgcc	ctggctaaag	ctactgtgaa	agaacttgcc	1620
tcactgcacg	gcaccaagta	cacatatggc	ccgggagcta	caacaatcta	tccttctgct	1680
gggacttcta	aagactgggc	ttatgaccaa	ggaatcagat	attccttcac	ctttgaactt	1740
cgagatacag	gcagatatgg	ctttctcctt	ccagaatccc	agatccgggc	tacctgcgag	1800
gagaccttcc	tggcaatcaa	gtatgttgcc	agctacgtcc	tggaacacct	gtactaataa	1860
tctagagaga						1870

<210> 113

<211> 613

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised Fd mutant HCPB sequence

<400> 113

Met Lys Leu Trp Leu Asn Trp Ile Phe Leu Val Thr Leu Leu Asn Gly
1 5 10 15

Ile Gln Cys Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg
20 25 30

Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile
35 40 45

Lys Asp Asn Tyr Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu
50 55 60

Glu Trp Ile Gly Trp Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala
65 70 75 80

Pro Lys Phe Arg Gly Arg Val Thr Met Leu Ala Asp Thr Ser Lys Asn
85 90 95

Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
100 105 110

Tyr Tyr Cys His Val Leu Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Gly Gly
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Thr Cys Asn Val
210 215 220

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Leu Lys
225 230 235 240

Thr Pro Leu Gly Asp Thr Thr His Thr Cys Pro Arg Cys Pro Glu Pro
245 250 255

Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu Pro Lys
260 265 270

Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu Pro Lys Ser
275 280 285

Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Ala Pro Glu Leu Leu
290 295 300

Gly Gly Ala Thr Gly His Ser Tyr Glu Lys Tyr Asn Lys Trp Glu Thr
305 310 315 320

Ile Glu Ala Trp Thr Gln Gln Val Ala Thr Glu Asn Pro Ala Leu Ile
325 330 335

Ser Arg Ser Val Ile Gly Thr Thr Phe Glu Gly Arg Ala Ile Tyr Leu
340 345 350

Leu Lys Val Gly Lys Ala Gly Gln Asn Lys Pro Ala Ile Phe Met Asp
355 360 365

Cys Gly Phe His Ala Arg Glu Trp Ile Ser Pro Ala Phe Cys Gln Trp
370 375 380

Phe	Val	Arg	Glu	Ala	Val	Arg	Thr	Tyr	Gly	Arg	Glu	Ile	Gln	Val	Thr	385	390	395	400
Glu	Leu	Leu	Asp	Lys	Leu	Asp	Phe	Tyr	Val	Leu	Pro	Val	Leu	Asn	Ile	405	410		415
Asp	Gly	Tyr	Ile	Tyr	Thr	Trp	Thr	Lys	Ser	Arg	Phe	Trp	Arg	Lys	Thr	420	425		430
Arg	Ser	Thr	His	Thr	Gly	Ser	Ser	Cys	Ile	Gly	Thr	Asp	Pro	Asn	Arg	435	440	445	
Asn	Phe	Asp	Ala	Gly	Trp	Cys	Glu	Ile	Gly	Ala	Ser	Arg	Asn	Pro	Cys	450	455	460	
Asp	Glu	Thr	Tyr	Cys	Gly	Pro	Ala	Ala	Glu	Ser	Glu	Lys	Glu	Thr	Lys	465	470	475	480
Ala	Leu	Ala	Asp	Phe	Ile	Arg	Asn	Lys	Leu	Ser	Ser	Ile	Lys	Ala	Tyr	485	490		495
Leu	Thr	Ile	His	Ser	Tyr	Ser	Gln	Met	Met	Ile	Tyr	Pro	Tyr	Ser	Tyr	500	505		510
Ala	Tyr	Lys	Leu	Gly	Glu	Asn	Asn	Ala	Glu	Leu	Asn	Ala	Leu	Ala	Lys	515	520	525	
Ala	Thr	Val	Lys	Glu	Leu	Ala	Ser	Leu	His	Gly	Thr	Lys	Tyr	Thr	Tyr	530	535	540	
Gly	Pro	Gly	Ala	Thr	Thr	Ile	Tyr	Pro	Ser	Ala	Gly	Thr	Ser	Lys	Asp	545	550	555	560
Trp	Ala	Tyr	Asp	Gln	Gly	Ile	Arg	Tyr	Ser	Phe	Thr	Phe	Glu	Leu	Arg	565	570		575
Asp	Thr	Gly	Arg	Tyr	Gly	Phe	Leu	Leu	Pro	Glu	Ser	Gln	Ile	Arg	Ala	580	585		590

Thr Cys Glu Glu Thr Phe Leu Ala Ile Lys Tyr Val Ala Ser Tyr Val
 595 600 605

Leu Glu His Leu Tyr
 610

<210> 114

<211> 96

<212> PRT

<213> Artificial Sequence

<220>

<223> preproHCPB with C-terminal Leu

<400> 114

His His Gly Gly Glu His Phe Glu Gly Glu Lys Val Phe Arg Val Asn
 1 5 10 15

Val Glu Asp Glu Asn His Ile Asn Ile Ile Arg Glu Leu Ala Ser Thr
 20 25 30

Thr Gln Ile Asp Phe Trp Lys Pro Asp Ser Val Thr Gln Ile Lys Pro
 35 40 45

His Ser Thr Val Asp Phe Arg Val Lys Ala Glu Asp Thr Val Thr Val
 50 55 60

Glu Asn Val Leu Lys Gln Asn Glu Leu Gln Tyr Lys Val Leu Ile Ser
 65 70 75 80

Asn Leu Arg Asn Val Val Glu Ala Gln Phe Asp Ser Arg Val Arg Leu
 85 90 95

<210> 115

<211> 520

<212> DNA

<213> Artificial Sequence

<220>

<223> chimaeric HuIgG3CH1' Fd construct

<400> 115

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ctctggggggc acagcggccc tgggctgcct ggtcaaggac tacttccccg aaccggtgac      120
ggtgtcgtgg aactcaggcg ccctgaccag cggcgtgcac accttccccg ctgtcctaca      180
gtcctcagga ctctactccc tcagcagcgt ggtgaccgtg ccctccagca gcttgggcac      240
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ggagctgaaa accccactcg gtgacacaa tcacacgtgc cctaggtgtc ctgaacctaa      360
atcttgtgac acacctcccc cgtgcccacg gtgcccagag cccaaatctt gcgacacgcc      420
cccaccgtgt ccagatgtc ctgaacaaaa gagctgtgac actccaccgc cctgcccgag      480
gtgcccagca cctgaactcc tgggagggtg atagcccggg      520
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<210> 116

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 116

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gttattactc gctgccaac cagccatggc g      31
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<210> 117

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 117

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23

<210> 118

<211> 88

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 118

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60

gtggtgatgg tggtggtaca ggtgttcc

88

<210> 119

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 119

caatctatcc tgctgctggg acttctaaag

30

<210> 120

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 120

gattggtgta gctcccgggc

20

<210> 121

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 121

ggagctacaa caatctatcc ttctgctggg

30

<210> 122

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer CME 00971

<400> 122

acggcaccaa gtacacatat gg

22

<210> 123

<211> 90

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer CME 00971

<400> 123

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gaaccgccac cgtacaggtg ttccaggacg 90

<210> 124

<211> 2154

<212> DNA

<213> Artificial Sequence

<220>

<223> humanised pre-pro HCPB-linker-Fd sequence

<400> 124

atgttggcac tcttggttct ggtgactgtg gccctggcat ctgctcatca tggtggtgag 60

cactttgaag gcgagaaggt gttccgtggt aacgttgaag atgaaaatca cattaacata 120

atccgcgagt tggccagcac gaccagatt gacttctgga agccagattc tgtcacacaa 180

atcaaacctc acagtacagt tgacttccgt gttaaagcag aagatactgt cactgtggag 240

aatgttctaa agcagaatga actacaatac aaggtactga taagcaacct gagaaatgtg 300

gtggaggctc agtttgatag ccgggttcgt gcaacaggac acagttatga gaagtacaac 360

aagtgggaaa cgatagaggc ttggactcaa caagtcgcca ctgagaatcc agccctcatc 420

tctcgcagtg ttatcggaac cacatttgag ggacgcgcta tttacctcct gaaggttggc 480

aaagctggac	aaaataagcc	tgccattttc	atggactgtg	gtttccatgc	cagagagtgg	540
atttctcctg	cattctgcca	gtggtttgta	agagaggctg	ttcgtaccta	tggacgtgag	600
atccaagtga	cagagcttct	cgacaagtta	gacttttatg	tcctgcctgt	gctcaatatt	660
gatggctaca	tctacacctg	gaccaagagc	cgatttttga	gaaagactcg	ctccacccat	720
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ccctccagca	gcttgggcac	ccagacctac	acctgcaacg	tgaatcacia	gccagcaac	1920
accaaggtgg	acaagagagt	ggagctgaaa	acccactcg	gtgacacaa	tcacacgtgc	1980
cctaggtgtc	ctgaacctaa	atcttgtgac	acacctcccc	cgtgccacag	gtgccagag	2040

cccaaattctt gcgacacgcc cccaccgtgt cccagatgtc ctgaaccaa gagctgtgac 2100
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<210> 125

<211> 716

<212> PRT

<213> Artificial Sequence

<220>

<223> humanised pre-pro HCPB-linker-Fd sequence

<400> 125

Met Leu Ala Leu Leu Val Leu Val Thr Val Ala Leu Ala Ser Ala His
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His Gly Gly Glu His Phe Glu Gly Glu Lys Val Phe Arg Val Asn Val
 20 25 30

Glu Asp Glu Asn His Ile Asn Ile Ile Arg Glu Leu Ala Ser Thr Thr
 35 40 45

Gln Ile Asp Phe Trp Lys Pro Asp Ser Val Thr Gln Ile Lys Pro His
 50 55 60

Ser Thr Val Asp Phe Arg Val Lys Ala Glu Asp Thr Val Thr Val Glu
 65 70 75 80

Asn Val Leu Lys Gln Asn Glu Leu Gln Tyr Lys Val Leu Ile Ser Asn
 85 90 95

Leu Arg Asn Val Val Glu Ala Gln Phe Asp Ser Arg Val Arg Ala Thr
 100 105 110

Gly His Ser Tyr Glu Lys Tyr Asn Lys Trp Glu Thr Ile Glu Ala Trp
 115 120 125

Thr	Gln	Gln	Val	Ala	Thr	Glu	Asn	Pro	Ala	Leu	Ile	Ser	Arg	Ser	Val	130	135	140	
Ile	Gly	Thr	Thr	Phe	Glu	Gly	Arg	Ala	Ile	Tyr	Leu	Leu	Lys	Val	Gly	145	150	155	160
Lys	Ala	Gly	Gln	Asn	Lys	Pro	Ala	Ile	Phe	Met	Asp	Cys	Gly	Phe	His	165	170	175	
Ala	Arg	Glu	Trp	Ile	Ser	Pro	Ala	Phe	Cys	Gln	Trp	Phe	Val	Arg	Glu	180	185	190	
Ala	Val	Arg	Thr	Tyr	Gly	Arg	Glu	Ile	Gln	Val	Thr	Glu	Leu	Leu	Asp	195	200	205	
Lys	Leu	Asp	Phe	Tyr	Val	Leu	Pro	Val	Leu	Asn	Ile	Asp	Gly	Tyr	Ile	210	215	220	
Tyr	Thr	Trp	Thr	Lys	Ser	Arg	Phe	Trp	Arg	Lys	Thr	Arg	Ser	Thr	His	225	230	235	240
Thr	Gly	Ser	Ser	Cys	Ile	Gly	Thr	Asp	Pro	Asn	Arg	Asn	Phe	Asp	Ala	245	250	255	
Gly	Trp	Cys	Glu	Ile	Gly	Ala	Ser	Arg	Asn	Pro	Cys	Asp	Glu	Thr	Tyr	260	265	270	
Cys	Gly	Pro	Ala	Ala	Glu	Ser	Glu	Lys	Glu	Thr	Lys	Ala	Leu	Ala	Asp	275	280	285	
Phe	Ile	Arg	Asn	Lys	Leu	Ser	Ser	Ile	Lys	Ala	Tyr	Leu	Thr	Ile	His	290	295	300	
Ser	Tyr	Ser	Gln	Met	Met	Ile	Tyr	Pro	Tyr	Ser	Tyr	Ala	Tyr	Lys	Leu	305	310	315	320
Gly	Glu	Asn	Asn	Ala	Glu	Leu	Asn	Ala	Leu	Ala	Lys	Ala	Thr	Val	Lys	325	330	335	

Glu Leu Ala Ser Leu His Gly Thr Lys Tyr Thr Tyr Gly Pro Gly Ala
340 345 350

Thr Thr Ile Tyr Pro Ser Ala Gly Thr Ser Lys Asp Trp Ala Tyr Asp
355 360 365

Gln Gly Ile Arg Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr Gly Arg
370 375 380

Tyr Gly Phe Leu Leu Pro Glu Ser Gln Ile Arg Ala Thr Cys Glu Glu
385 390 395 400

Thr Phe Leu Ala Ile Lys Tyr Val Ala Ser Tyr Val Leu Glu His Leu
405 410 415

Tyr Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln
420 425 430

Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Gln Thr Leu Ser
435 440 445

Leu Thr Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asn Tyr Met His
450 455 460

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly Trp Ile
465 470 475 480

Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Lys Phe Arg Gly Arg
485 490 495

Val Thr Met Leu Ala Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg Leu
500 505 510

Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys His Val Leu
515 520 525

Ile Tyr Ala Gly Tyr Leu Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
530 535 540

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
545 550 555 560

Ala Pro Cys Ser Arg Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
565 570 575

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
580 585 590

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
595 600 605

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
610 615 620

Leu Gly Thr Gln Thr Tyr Thr Cys Asn Val Asn His Lys Pro Ser Asn
625 630 635 640

Thr Lys Val Asp Lys Arg Val Glu Leu Lys Thr Pro Leu Gly Asp Thr
645 650 655

Thr His Thr Cys Pro Arg Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro
660 665 670

Pro Pro Cys Pro Arg Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro
675 680 685

Pro Cys Pro Arg Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro
690 695 700

Cys Pro Arg Cys Pro Ala Pro Glu Leu Leu Gly Gly
705 710 715

<210> 126

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 126

tatataaagc ttgccgccac catgggccac acacggaggc ag

42

<210> 127

<211> 45

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 127

actccaccag cttcacctcg ttatcaggaa aatgctcttg cttgg

45

<210> 128

<211> 45

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 128

agagcatttt cctgataacg aggtgaagct ggtggagtct ggagg

45

<210> 129

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer for mutant HCPB

<400> 129

ccaggcatcc cagggtcacc atggagttag tttgggcagc

40

<210> 130

<211> 1446

<212> DNA

<213> Artificial Sequence

<220>

<223> full-length human B7.1-murine ASB7 Fd fusion

<220>

<221> CDS

<222> (16)..(1434)

<223>

<400> 130

aagcttgccg ccacc atg ggc cac aca cgg agg cag gga aca tca cca tcc 51
Met Gly His Thr Arg Arg Gln Gly Thr Ser Pro Ser
1 5 10

aag tgt cca tac ctc aat ttc ttt cag ctc ttg gtg ctg gct ggt ctt 99
Lys Cys Pro Tyr Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu
15 20 25

tct cac ttc tgt tca ggt gtt atc cac gtg acc aag gaa gtg aaa gaa 147
Ser His Phe Cys Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu
30 35 40

gtg gca acg ctg tcc tgt ggt cac aat gtt tct gtt gaa gag ctg gca 195
Val Ala Thr Leu Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala
45 50 55 60

caa act cgc atc tac tgg caa aag gag aag aaa atg gtg ctg act atg 243

Gln	Thr	Arg	Ile	Tyr 65	Trp	Gln	Lys	Glu	Lys 70	Lys	Met	Val	Leu	Thr 75	Met		
atg	tct	ggg	gac	atg	aat	ata	tgg	ccc	gag	tac	aag	aac	cgg	acc	atc	291	
Met	Ser	Gly	Asp	Met	Asn	Ile	Trp	Pro	Glu	Tyr	Lys	Asn	Arg	Thr	Ile		
			80					85					90				
ttt	gat	atc	act	aat	aac	ctc	tcc	att	gtg	atc	ctg	gct	ctg	cgc	cca	339	
Phe	Asp	Ile	Thr	Asn	Asn	Leu	Ser	Ile	Val	Ile	Leu	Ala	Leu	Arg	Pro		
		95					100					105					
tct	gac	gag	ggc	aca	tac	gag	tgt	gtt	gtt	ctg	aag	tat	gaa	aaa	gac	387	
Ser	Asp	Glu	Gly	Thr	Tyr	Glu	Cys	Val	Val	Leu	Lys	Tyr	Glu	Lys	Asp		
	110					115					120						
gct	ttc	aag	cgg	gaa	cac	ctg	gct	gaa	gtg	acg	tta	tca	gtc	aaa	gct	435	
Ala	Phe	Lys	Arg	Glu	His	Leu	Ala	Glu	Val	Thr	Leu	Ser	Val	Lys	Ala		
125					130					135					140		
gac	ttc	cct	aca	cct	agt	ata	tct	gac	ttt	gaa	att	cca	act	tct	aat	483	
Asp	Phe	Pro	Thr	Pro	Ser	Ile	Ser	Asp	Phe	Glu	Ile	Pro	Thr	Ser	Asn		
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Ile	Arg	Arg	Ile	Ile	Cys	Ser	Thr	Ser	Gly	Gly	Phe	Pro	Glu	Pro	His		
			160					165					170				
ctc	tcc	tgg	ttg	gaa	aat	gga	gaa	gaa	tta	aat	gcc	atc	aac	aca	aca	579	
Leu	Ser	Trp	Leu	Glu	Asn	Gly	Glu	Glu	Leu	Asn	Ala	Ile	Asn	Thr	Thr		
		175					180					185					
gtt	tcc	caa	gat	cct	gaa	act	gag	ctc	tat	gct	gtt	agc	agc	aaa	ctg	627	
Val	Ser	Gln	Asp	Pro	Glu	Thr	Glu	Leu	Tyr	Ala	Val	Ser	Ser	Lys	Leu		
	190					195				200							
gat	ttc	aat	atg	aca	acc	aac	cac	agc	ttc	atg	tgt	ctc	atc	aag	tat	675	
Asp	Phe	Asn	Met	Thr	Thr	Asn	His	Ser	Phe	Met	Cys	Leu	Ile	Lys	Tyr		
205					210				215					220			
gga	cat	tta	aga	gtg	aat	cag	acc	ttc	aac	tgg	aat	aca	acc	aag	caa	723	
Gly	His	Leu	Arg	Val	Asn	Gln	Thr	Phe	Asn	Trp	Asn	Thr	Thr	Lys	Gln		
				225					230					235			
gag	cat	ttt	cct	gat	aac	gag	gtg	aag	ctg	gtg	gag	tct	gga	gga	ggc	771	
Glu	His	Phe	Pro	Asp	Asn	Glu	Val	Lys	Leu	Val	Glu	Ser	Gly	Gly	Gly		
			240					245					250				
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Leu	Val	Gln	Pro	Gly	Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Thr	Ser	Gly		
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Lys	Ala	Leu	Glu	Trp	Leu	Gly	Phe	Ile	Gly	Asn	Lys	Ala	Asn	Gly	Tyr	
285					290					295					300	
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Thr	Thr	Glu	Tyr	Ser	Ala	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	
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Asp	Lys	Ser	Gln	Ser	Ile	Leu	Tyr	Leu	Gln	Met	Asn	Thr	Leu	Arg	Ala	
			320					325					330			
gag	gac	agt	gcc	act	tat	tac	tgt	aca	aga	gat	agg	ggg	cta	cgg	ttc	1059
Glu	Asp	Ser	Ala	Thr	Tyr	Tyr	Cys	Thr	Arg	Asp	Arg	Gly	Leu	Arg	Phe	
		335					340					345				
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Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Thr	Leu	Thr	Val	Ser	Ser	Ala	
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Lys	Thr	Thr	Pro	Pro	Ser	Val	Tyr	Pro	Leu	Ala	Pro	Gly	Ser	Ala	Ala	
365					370				375						380	
caa	act	aac	tcc	atg	gtg	acc	ctg	gga	tgc	ctg	gtc	aag	ggc	tat	ttc	1203
Gln	Thr	Asn	Ser	Met	Val	Thr	Leu	Gly	Cys	Leu	Val	Lys	Gly	Tyr	Phe	
				385					390					395		
cct	gag	cca	gtg	aca	gtg	acc	tgg	aac	tct	gga	tct	ctg	tcc	agc	ggg	1251
Pro	Glu	Pro	Val	Thr	Val	Thr	Trp	Asn	Ser	Gly	Ser	Leu	Ser	Ser	Gly	
			400					405					410			
gtg	cac	acc	ttc	cca	gct	gtc	ctg	cag	tct	gac	ctc	tac	act	ctg	agc	1299
Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Asp	Leu	Tyr	Thr	Leu	Ser	
		415					420					425				
agc	tca	gtg	act	gtc	ccc	tcc	agc	acc	tgg	ccc	agc	gag	acc	gtc	acc	1347
Ser	Ser	Val	Thr	Val	Pro	Ser	Ser	Thr	Trp	Pro	Ser	Glu	Thr	Val	Thr	
	430					435					440					
tgc	aac	gtt	gcc	cac	ccg	gcc	agc	agc	acc	aag	gtg	gac	aag	aaa	att	1395
Cys	Asn	Val	Ala	His	Pro	Ala	Ser	Ser	Thr	Lys	Val	Asp	Lys	Lys	Ile	
445					450					455					460	
gtg	ccc	agg	gat	tgt	ggg	tgt	aag	cct	tgc	ata	tgt	aca	tagtaagaat	tc		1446
Val	Pro	Arg	Asp	Cys	Gly	Cys	Lys	Pro	Cys	Ile	Cys	Thr				
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<211> 473

<212> PRT

<213> Artificial Sequence

<220>

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<400> 131

Met Gly His Thr Arg Arg Gln Gly Thr Ser Pro Ser Lys Cys Pro Tyr
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Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu Ser His Phe Cys
20 25 30

Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
35 40 45

Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
50 55 60

Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
65 70 75 80

Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
85 90 95

Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly
100 105 110

Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
115 120 125

Glu His Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr
130 135 140

Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile
145 150 155 160

Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
165 170 175

Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp
180 185 190

Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met
195 200 205

Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
210 215 220

Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro
225 230 235 240

Asp Asn Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
245 250 255

Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Thr
260 265 270

Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Ala Leu Glu
275 280 285

Trp Leu Gly Phe Ile Gly Asn Lys Ala Asn Gly Tyr Thr Thr Glu Tyr
290 295 300

Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Lys Ser Gln
305 310 315 320

Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Arg Ala Glu Asp Ser Ala
325 330 335

Thr Tyr Tyr Cys Thr Arg Asp Arg Gly Leu Arg Phe Tyr Phe Asp Tyr
340 345 350

Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Ala Lys Thr Thr Pro
355 360 365

Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala Ala Gln Thr Asn Ser
370 375 380

Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val
385 390 395 400

Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe
405 410 415

Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr
420 425 430

Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val Thr Cys Asn Val Ala
435 440 445

His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Val Pro Arg Asp
450 455 460

Cys Gly Cys Lys Pro Cys Ile Cys Thr
465 470